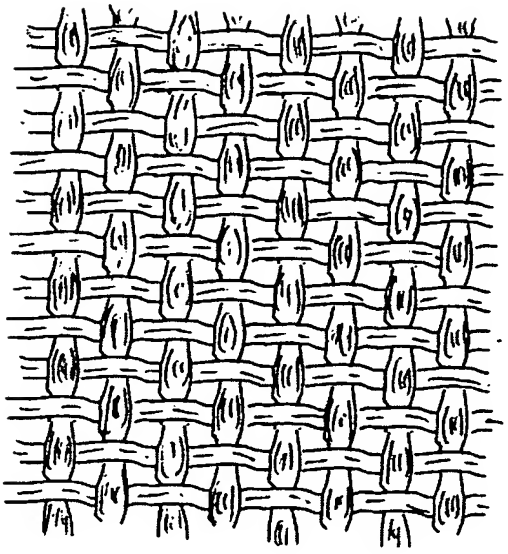


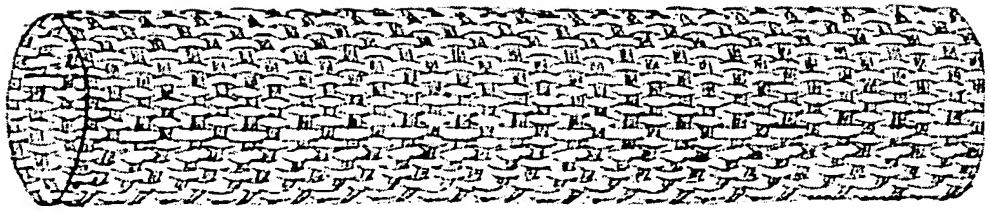


FIGURE 1

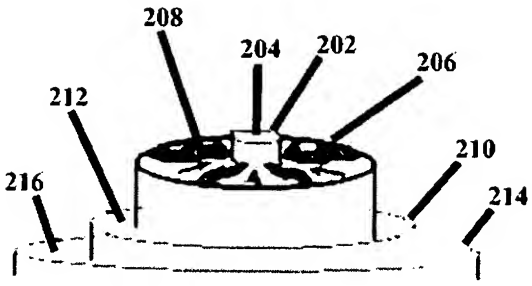


FIGURE 2A

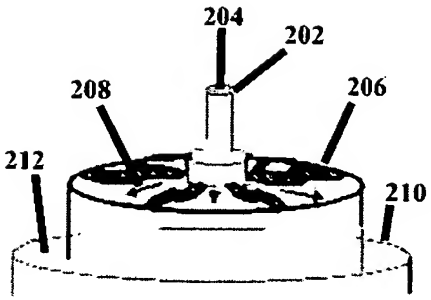


FIGURE 2B

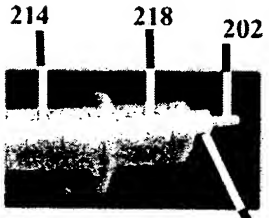


FIGURE 2C

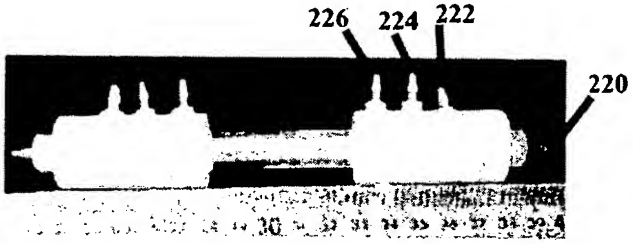


FIGURE 2D

FIGURE 2

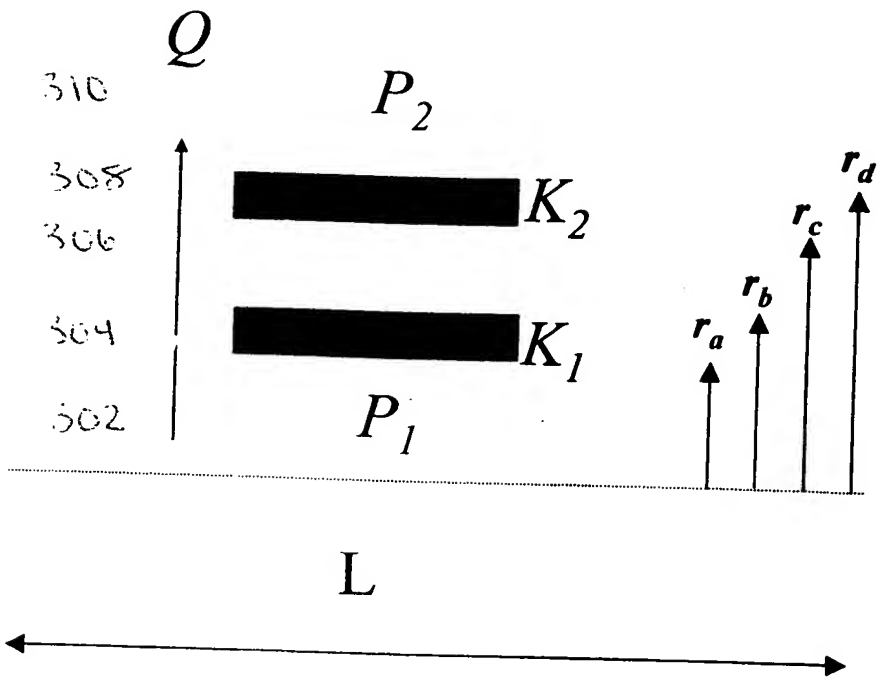
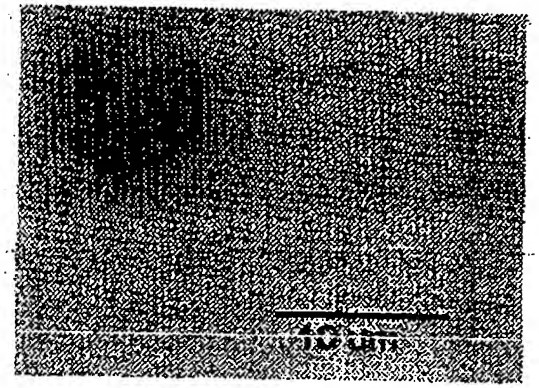
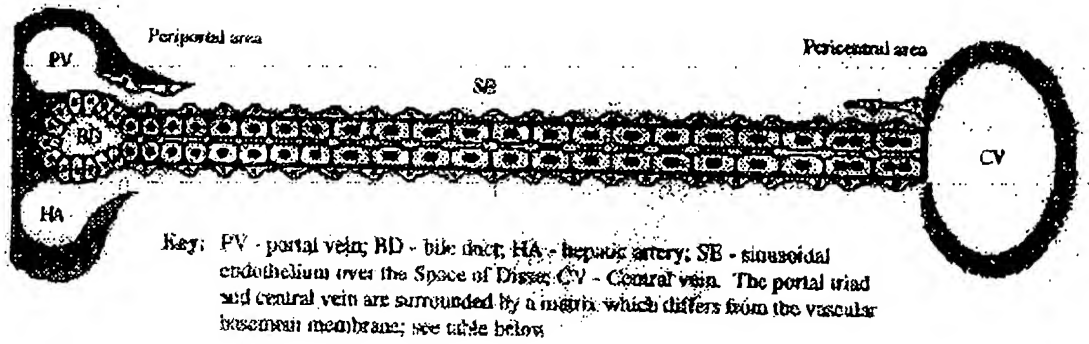


Figure 3

Liver Lineage Model

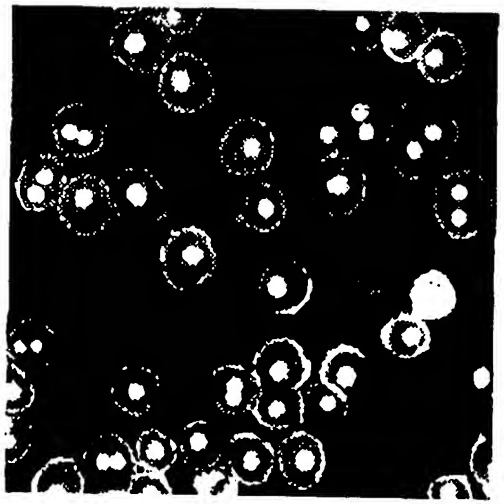
HUMAN LIVER PROGENITORS





Key: PV - portal vein; BD - bile duct; HA - hepatic artery; SE - sinusoidal endothelium over the Space of Disse; CV - Central vein. The portal triad and central vein are surrounded by a matrix which differs from the vascular basement membrane; see table below

HUMAN ADULTS HEPATOCYTES



Zones	1	2	3
Ploidy	**Diploid**	**Tetraploid**	**Octaploid**
Size	**7-20 *u***	**20-35 *u***	**35-50 u**
Growth	**maximum**	**limited**	**negligible**
ECM	**Type IV collagen Laminin, HS-PG**	**>>>>>>>>>>>>>>>>>>>>>> Gradient**	**Fibrillar collagens Fibronectin, HP-PG**
Genes	**early**	**intermediate**	**late**

Figure 4

Multicoaxial Bioreactor Design

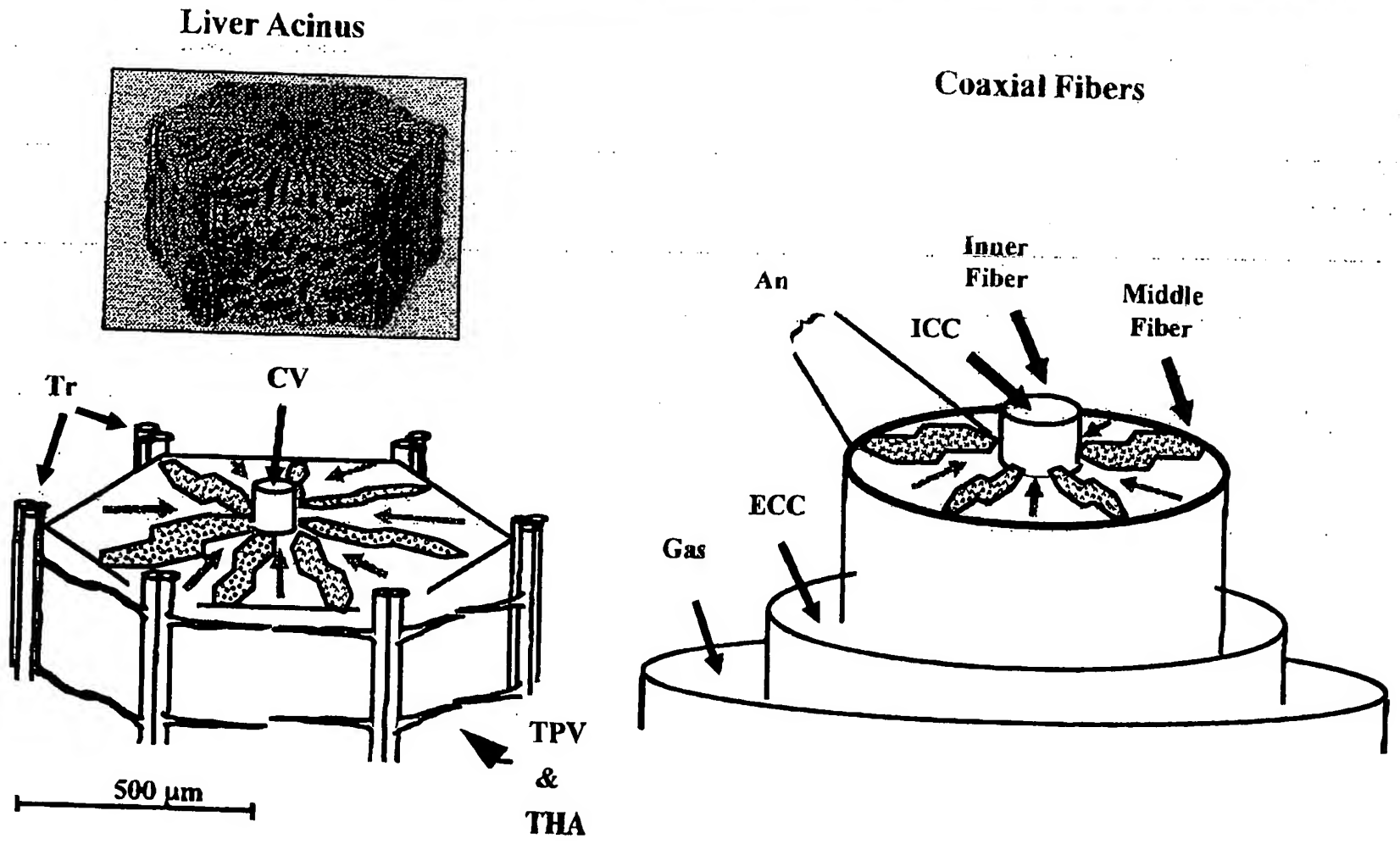


Figure 5

Porous, Biocompatible, Biodegradable PLGA Microcarriers for Cells in Bioreactors

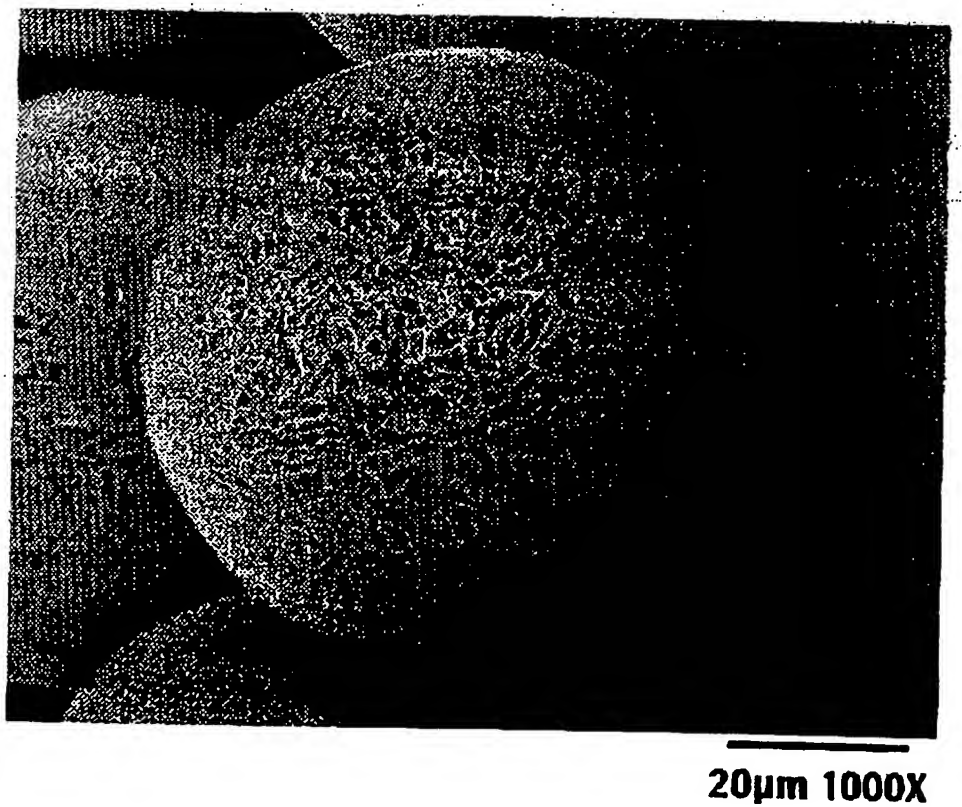


Figure 6

Physical Analysis of the Liver Acinus

Components of Mass Transfer:

$$\underbrace{\partial c/\partial t}_{\text{Gas, Nutrient or Metablite Profile or Map}} = \underbrace{D\nabla^2 c}_{\text{Diffusion}} + \underbrace{\underline{v}\bullet \nabla c}_{\text{Convection}} + \underbrace{R}_{\text{Metabolism}}$$

Diffusion (10^{-6} cm^2/s; 200 μm)

Convection ($140\text{-}10^{-2}$ cm/s; meters)

Metabolism (0.5 nmol $O_2/s/10^6$ cells)

- **PORTAL TRIAD**
  - Portal venule
  - Hepatic arteriole
  - Bile ductule
  - Lymph vessel

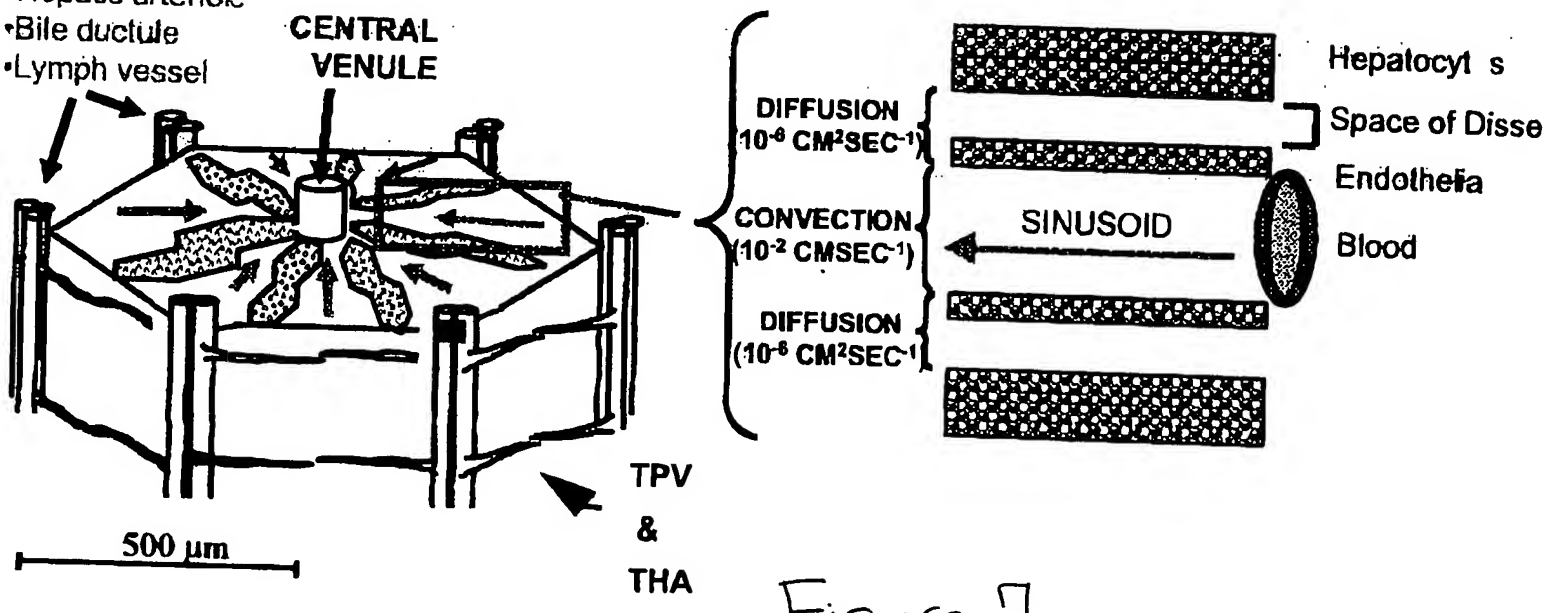
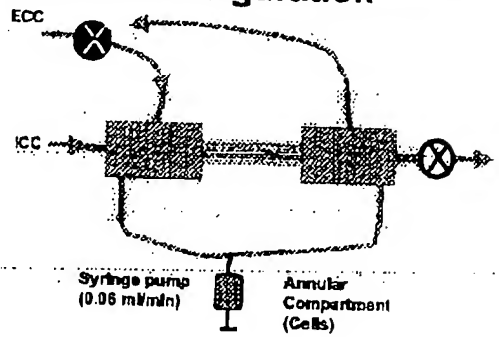


Figure 7

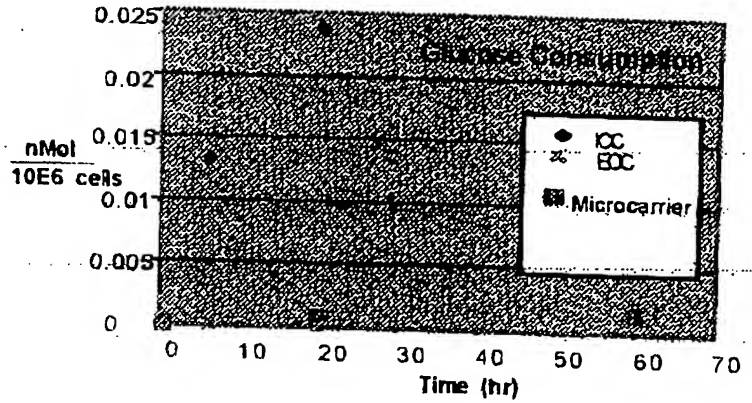
Membrane 'Fouling' Studies

CELL STUDY OF DEAD-ENDED FLOW

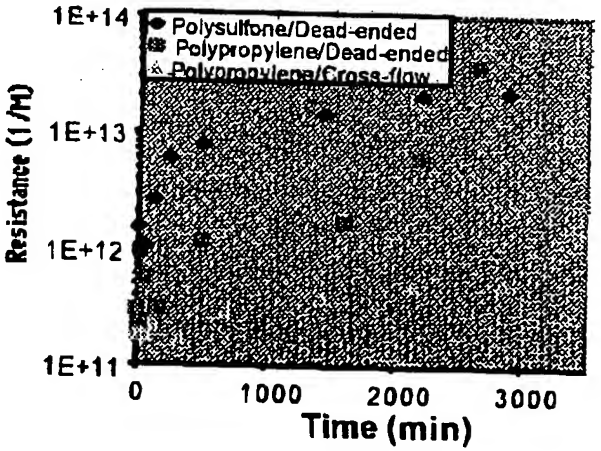
Flow Configuration



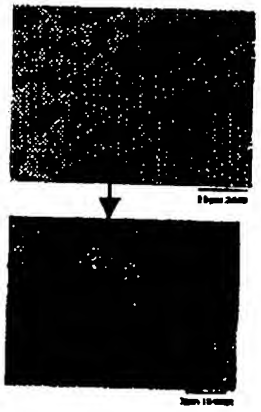
HepG2 Cells



STUDY OF \FIBER AND FLOW TYPE



Polysulfone Dead-ended Flow

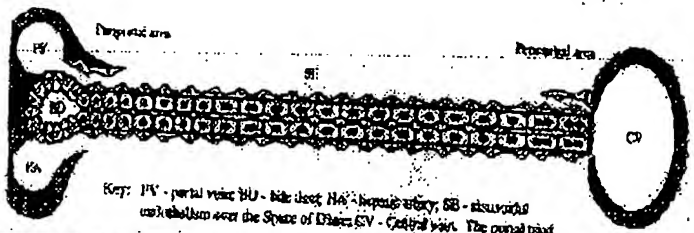


Polypropylene Dead-ended Fl w

Figure 8

Effect of No Hemoglobin on Oxygen Mass Transfer (O_2 Gradients)

pO_2 (mmHg)	70	20
Hb-Bound	6.26 mM	2.91 mM
Free	0.1 mM	0.03 mM



- Clotting factors - 'fouling'
  Perflourinated hydrocarbons are peroxisome proliferators
  Synthetically modified hemoglobin blood substitutes that lack function: cooperativity.

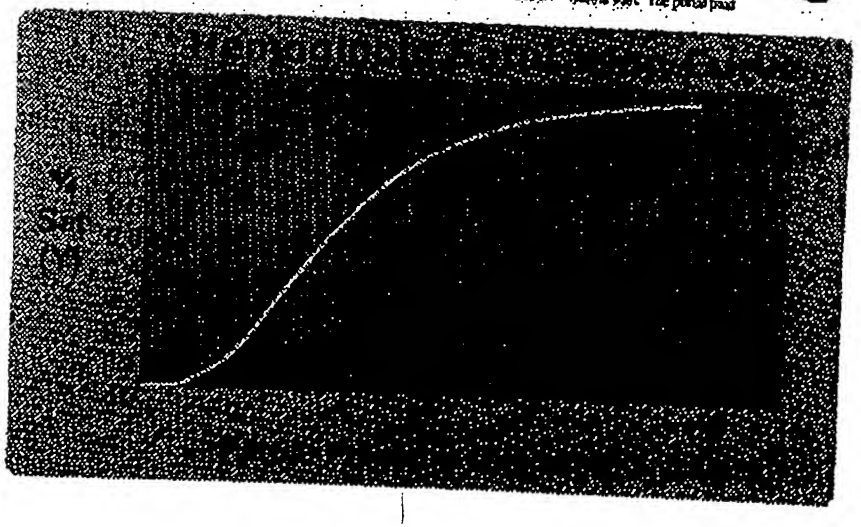
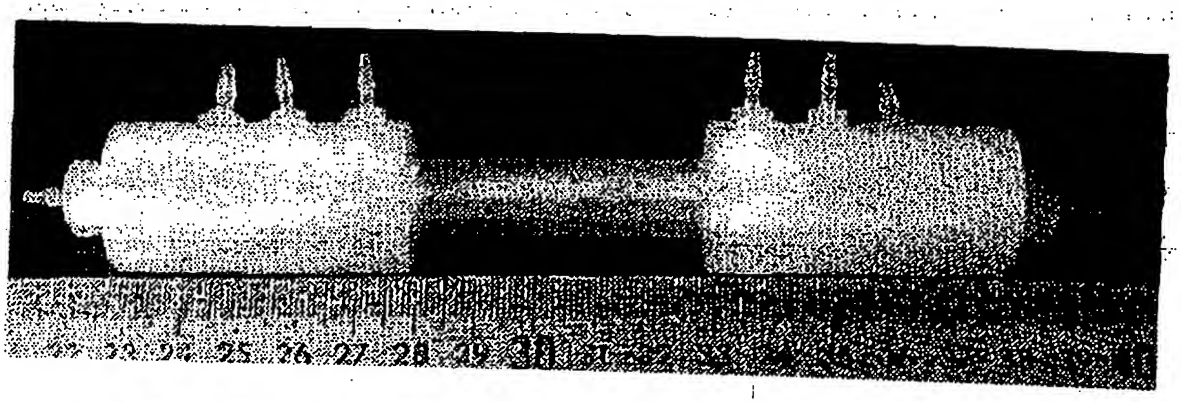


Figure 9

Comparison of Conventional and Our Multicoaxial Bioreactor

Multicoaxial



Conventional

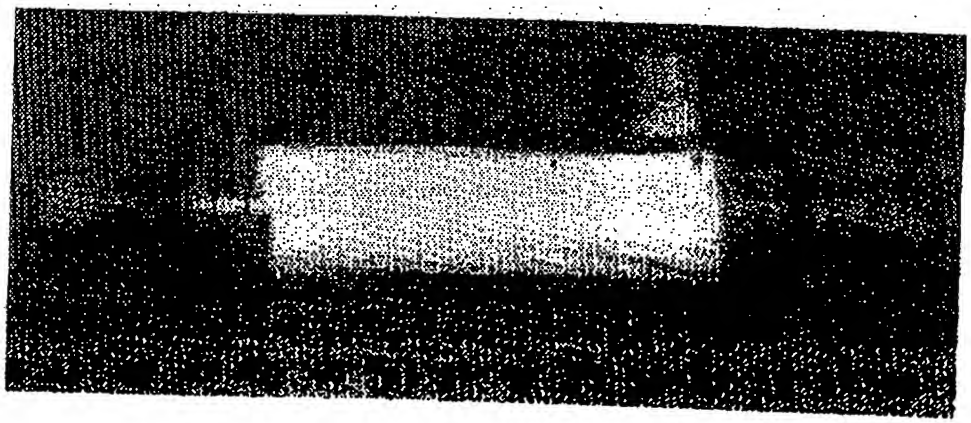


Figure 10

RESULTS

Hydrodynamic Model

Darcy's Law, $v = -K\nabla P$.

$$\Delta P = \frac{Q}{2\pi L}\left[\frac{\ln\left(\frac{r_b}{r_a}\right)}{K_1} - \frac{\ln\left(\frac{r_d}{r_c}\right)}{K_2}\right]$$

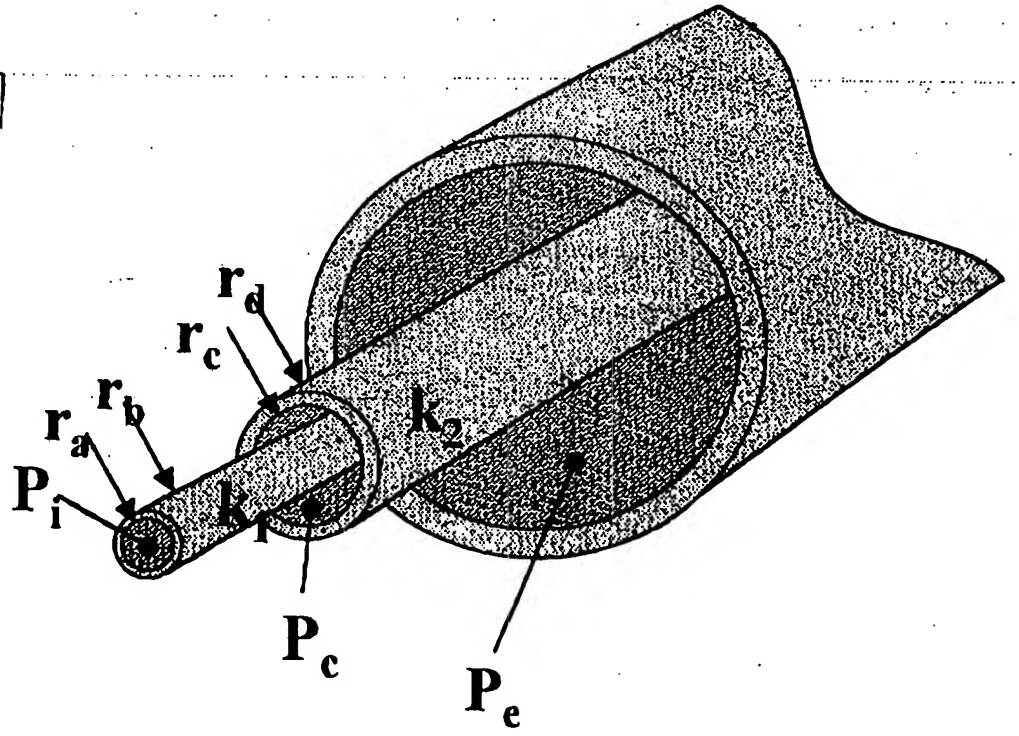
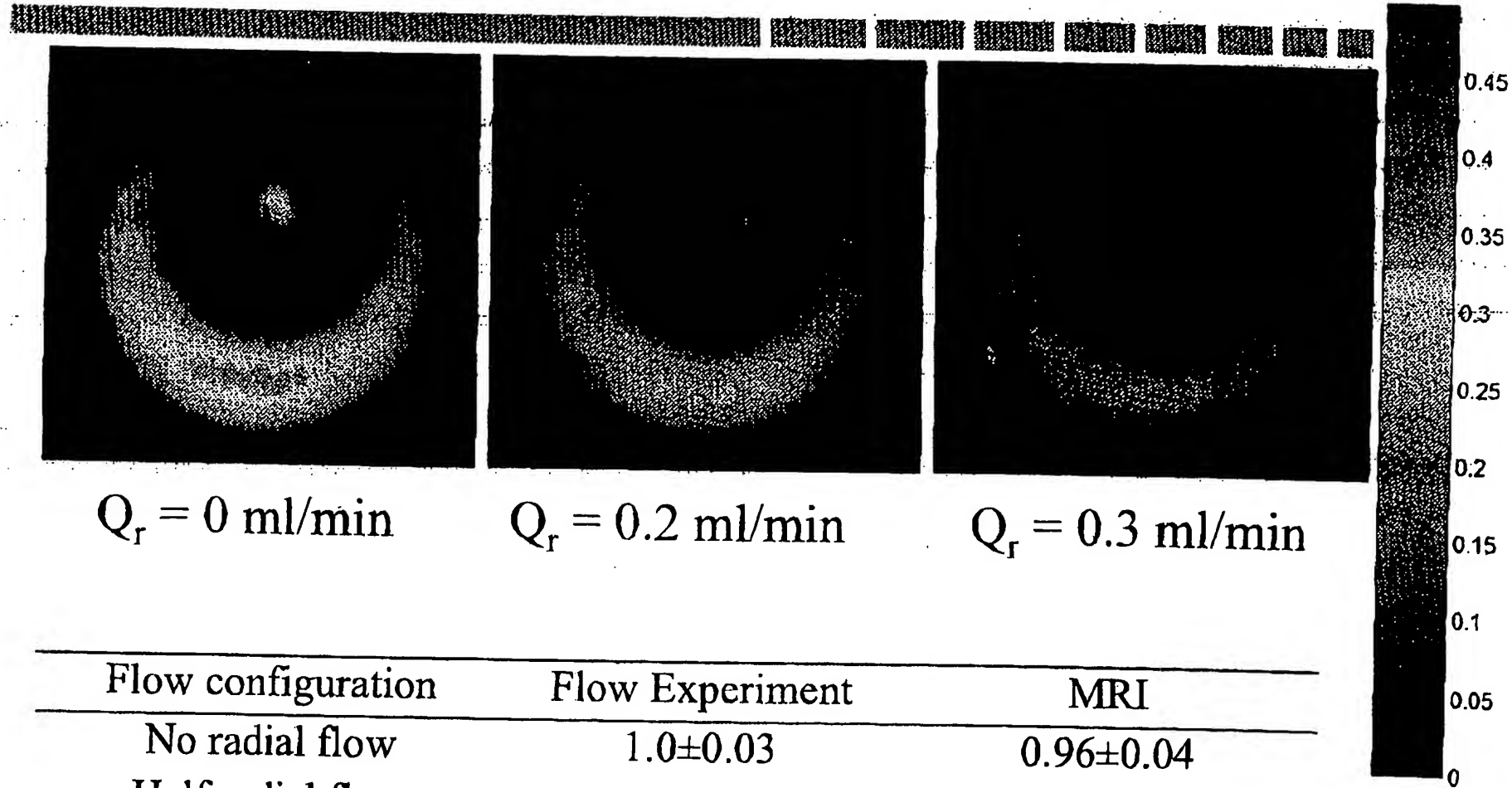


Figure 11

MRI used to determine axial flow



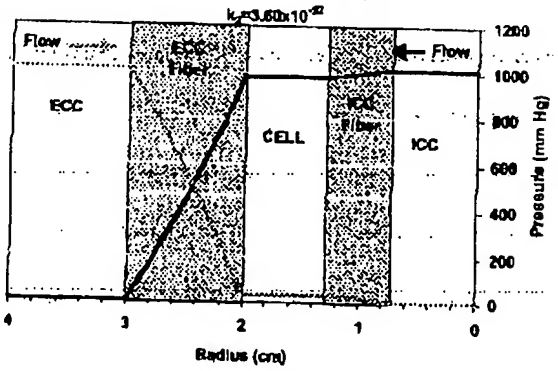
$Q_r = 0$ ml/min $Q_r = 0.2$ ml/min $Q_r = 0.3$ ml/min

Flow configuration	Flow Experiment	MRI
No radial flow	1.0±0.03	0.96±0.04
Half radial flow	0.70±0.02	0.68±0.03
Full radial flow	0.50±0.04	0.52±0.03

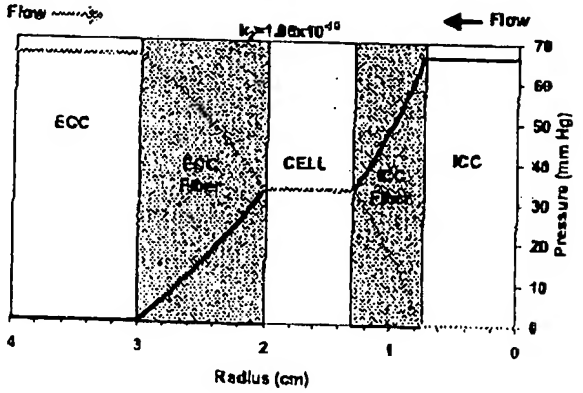
Figure 12

Predicted Pressure Profile and Optimum K_1 and K_2

Commercially Available Fibers



Predict Upper Range Using the Model



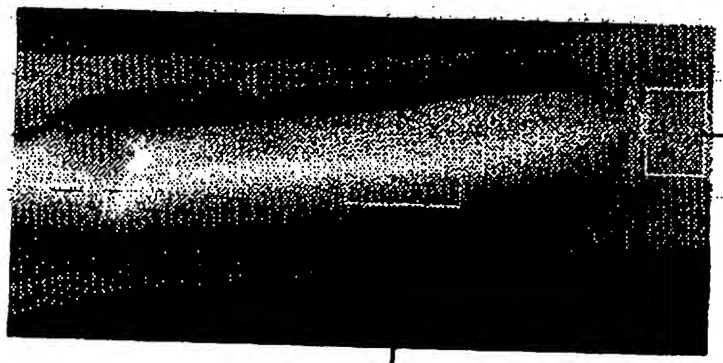
Pressure Threshold Range-finding

VIABILITY	PRESSURE
40%	517
70%	258
100%	103

Average Pressure in Sinusoid = 5-10 mm Hg
Average Sinusoidal Blood Flow = 0.01 cm/sec

Figure 13

Membrane 'Fouling' and Adverse Effect on Mass Transfer



Middle Fiber
(0.1 µm pores)

Inner Fiber
(0.65 µm pores)

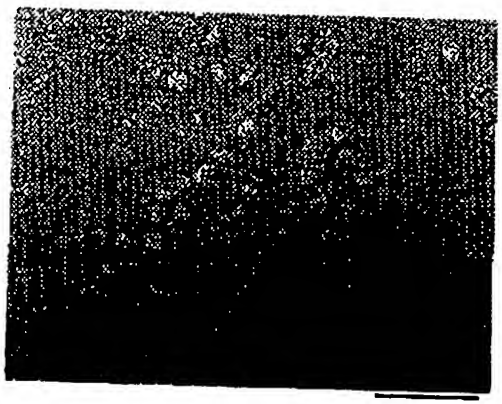
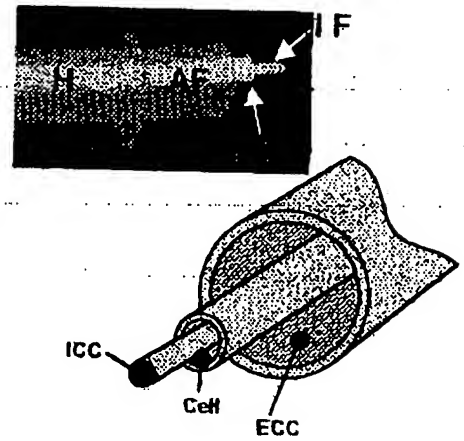


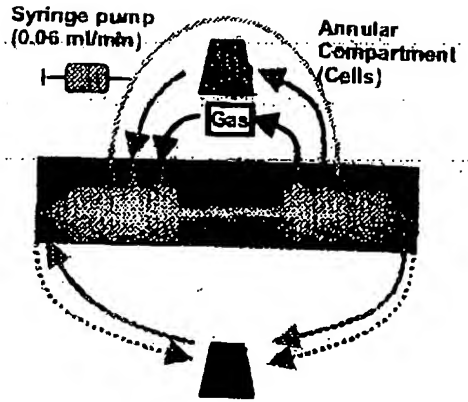
Figure 14

Dead-end and Cross Flow Configurations for the Fouling Study

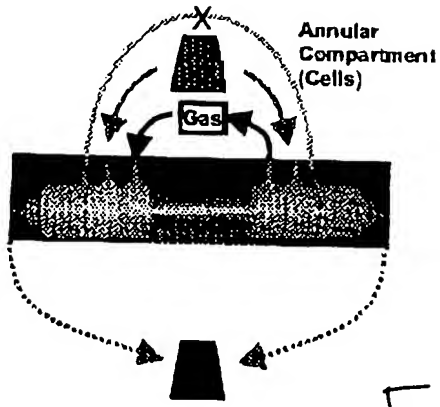
Multicoaxial Bioreactor



Direct Dead-ended Flow Configuration



Dead-ended Flow Configuration



Cross Flow Configuration

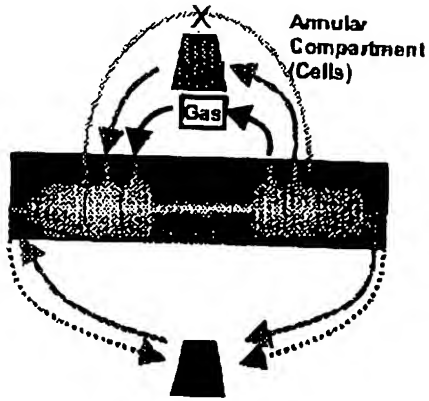
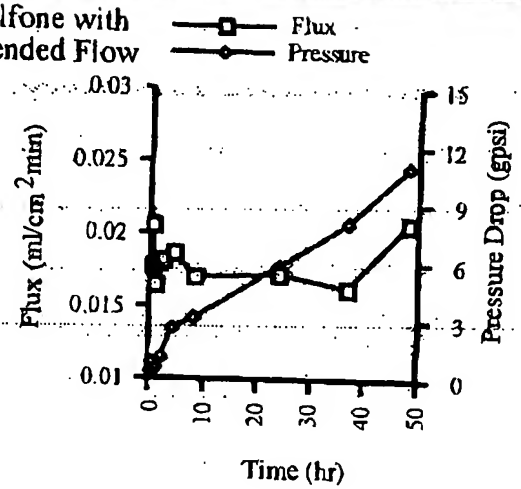
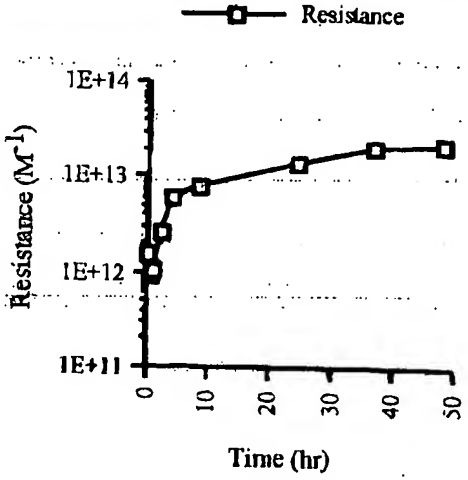


Figure 15

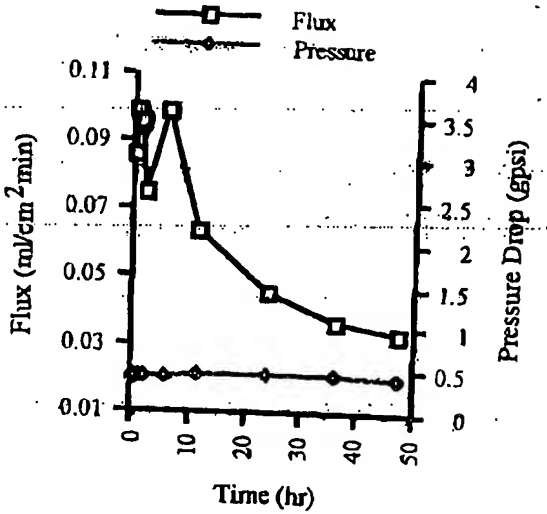
Results of the Dead-end and Cross Flow Configurations for the Fouling Study

Polysulfone with Dead-ended Flow

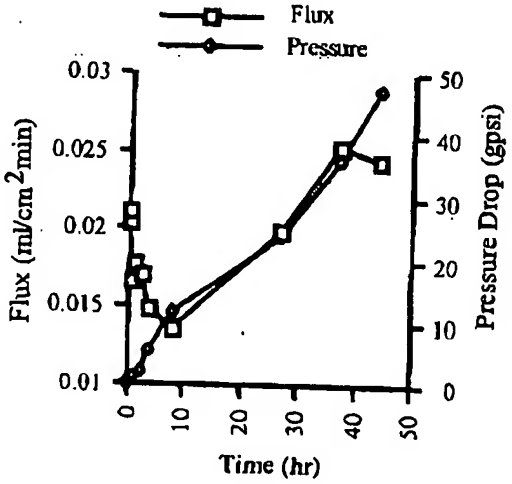


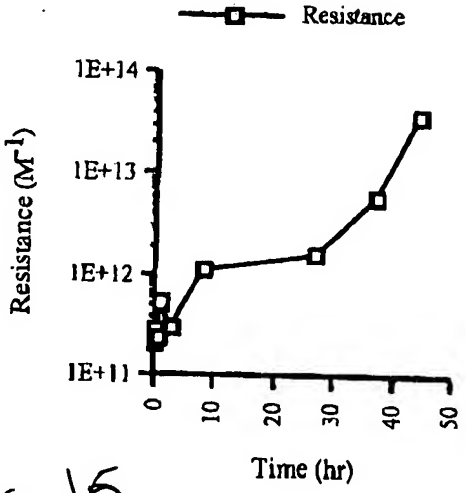


Polypropylene with Cross Flow



Polypropylene with Dead-ended Flow





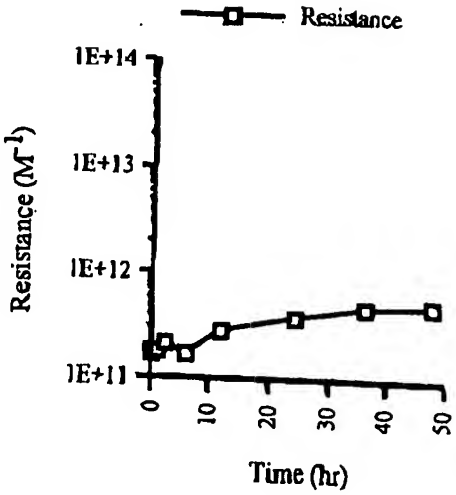


Figure 16

Results of the Dead-end and Cross Flow Configurations for the Fouling Study

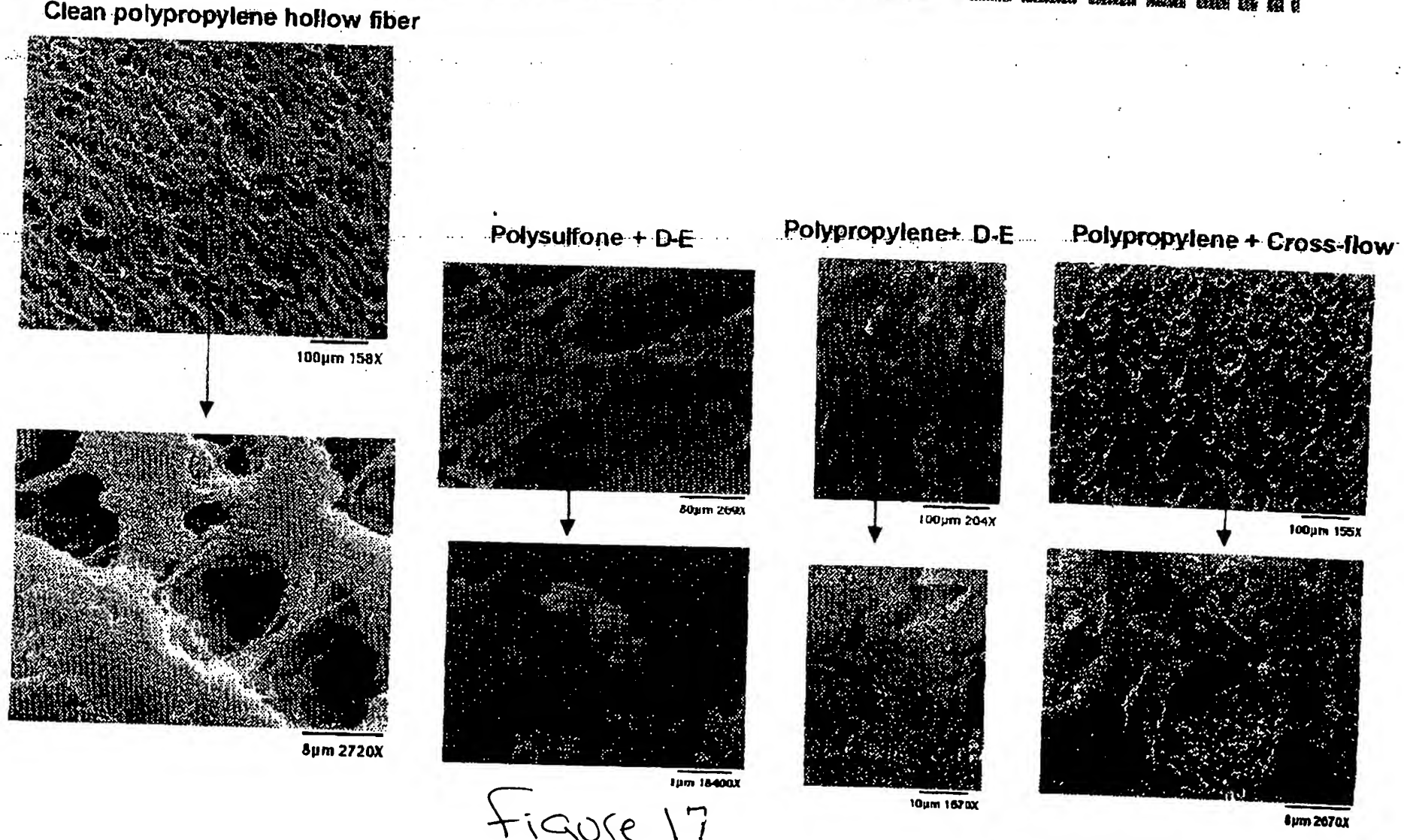
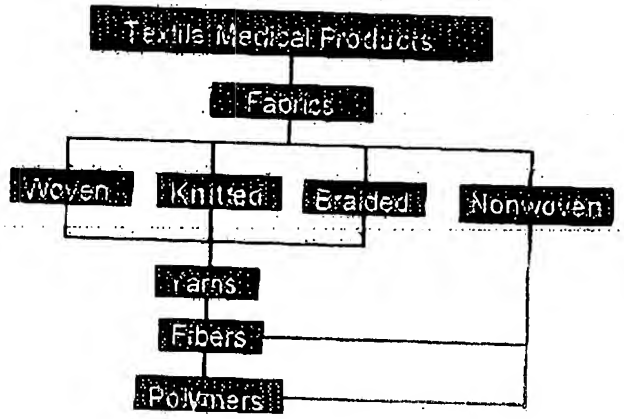
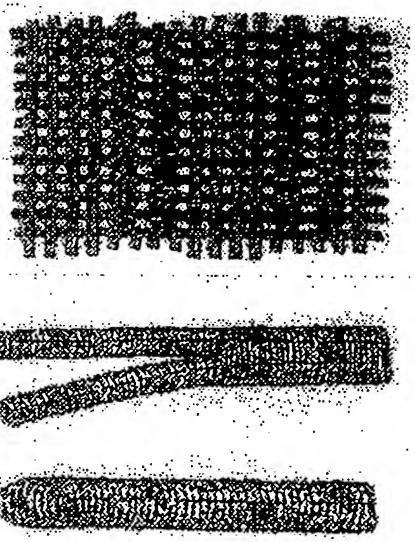
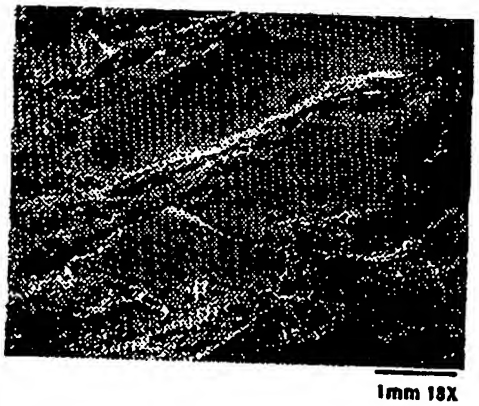


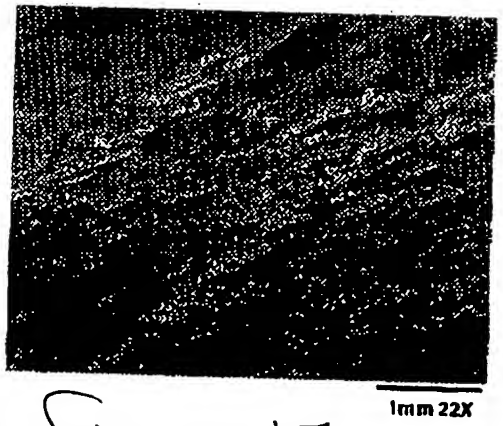
Figure 17

Fouling Studies of Woven Vasculature Incorporated into Multicoaxial Bioreactors









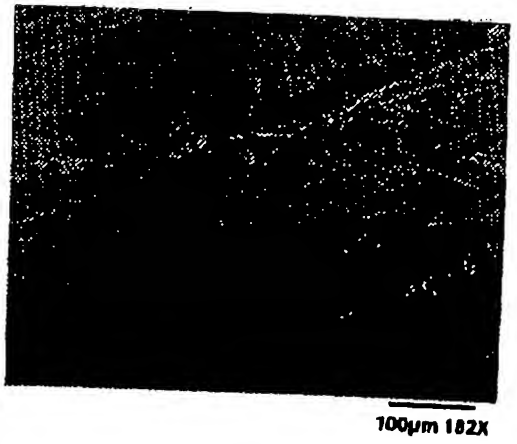


figure 18